REMARKS

Claim 10, as herein amended, claims 13-15, as previously presented, and claims 11, 12, 18-20 and 23 as filed are pending in the application. Claims 1-9, 16, 17, 21, 22, 24-36 are cancelled without prejudice or disclaimer, for pursuit in related applications.

Applicant acknowledges with gratitude withdrawal of all previously-asserted grounds of rejection. The rejections asserted in the Office Action have been overcome by amendment or traversed by argument. No new matter is introduced by the amendments submitted herewith, which are fully supported by the specification as filed.

1. The claims as amended are non-obvious over the cited prior art.

Claims 10-15, 18-20 and 23 stand rejected as being obvious under 35 U.S.C. §103 over the teachings of the Kopreski reference combined with the teachings of Mok as previously asserted and newly in combination with the teachings of the newly-asserted Kang reference (in the Chinese language but with an English language abstract). The teachings of the Kopreski and Mok references (including the deficiencies thereof) were extensively discussed in response to the previously-asserted rejections on obviousness grounds and will not be repeated here. The Action newly asserts the Kang reference as evidence that the art taught the existence of apoptotic bodies in pleural effusions, specifically on page 4 of the Action, that "Kang et al. disclose a method of analyzing pleural effusions from a lung carcinoma patient and identifying that apoptotic bodies are present in the fluid." The Action also continues to assert that Kopreski "inherently" detected RNA from apoptotic bodies by performing the claimed methods as described in the instant specification.

With regard to the newly-asserted Kang reference, Applicant has carefully reviewed the English-language Abstract and can find no statement that apoptotic bodies were found in pleural effusions. What the Kang abstract states is that "[f]low cytometry, optical microscopy, electron microscopy, and TUNEL method were used to compare the cytology and biochemistry of pleural effusion and cancer cells planted on the surface of pleura before and after the therapy" (emphasis added). Applicant respectfully highlights that no mention is made in the abstract of apoptotic bodies in pleural effusion *prior to* therapy. After therapy, only one patient developed recurrence of pleural effusion. However, the Kang reference does not disclose anything regarding apoptotic bodies in the

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pleural effusion of this patient, just that "no carcinoma cell was found in pleural effusion." Kang then affirmatively states that "[p]yknosis and disintegration of nuclei, and apoptotic bodies of tumor cells planted on the surface of pleura were found by optical and electron microscopy" (abstract; *emphasis underlined*). Thus, a careful review of the Kang abstract provides no statement that apoptotic bodies were detected in the pleural effusion fluid itself. Rather, apoptotic bodies of cells on the surface of the pleura were found, which surfaces are not interrogated using Applicant's claimed methods.

Moreover, the Kang abstract reports that apoptotic bodies were found in patients only *after* a specific treatment that directly exposes tumor cells on the pleural wall to a treatment – interpleural hyperthermic effusion. This treatment was directed towards treating malignant pleural effusion caused by lung cancer, which was successful in 44/45 cases (i.e., the malignant pleural effusion did not recur, according to the Kang Abstract). The Abstract further reports that patients receiving this treatment showed apoptosis in carcinoma cells deposited on the pleural wall. Applicant respectfully contends that even if the Kang Abstract can be interpreted as showing that apoptotic bodies can be found in pleural effusions, which Applicant respectfully contends it cannot, the skilled worker would recognize that the Abstract indicates said apoptotic bodies are produced as the result of this specific direct treatment, and provides no expectation that apoptotic bodies can be found generally in pleural effusions.

Applicant further respectfully highlights that even if the Kang reference detected apoptotic bodies in pleural effusion, which Applicant respectfully contends is not supported by the abstract, the instant claims are not solely limited by detecting apoptotic bodies in pleural effusion. Rather, they provide methods for "extracting, separating, isolating, or purifying an apoptotic body" from pleural effusion. Kang et al. in their abstract do not indicate that they provide any method for extracting, separating, isolating, or purifying an apoptotic body from pleural effusion. Indeed, the reference only teaches that such apoptotic bodies can be detected on the pleural surface. The Kopreski reference does not cure this deficiency, since even with regard to serum Kopreski provides no teaching directed to methods for isolating apoptotic bodies from serum, but applies centrifugation only to isolate serum from the cellular components of the blood specimen. Thus, Applicant respectfully contends that the combination of the Kopreski reference and the Kang abstract do not teach methods for separating or isolating apoptotic bodies from a bodily fluid as taught in the instant specification. These claimed methods advantageously improve the ability to extract or analyze RNA

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or other compositions present in the apoptotic bodies, something not found in nor suggested by the cited art.

Lastly, although Kopreski et al. indicate that apoptotic bodies in serum contain RNA, the Kang abstract provides no indication that apoptotic bodies in pleural effusion contain RNA.

As set forth in their prior response, and inherently acknowledged in the Action, the Mok reference does not cure these difficulties, since it is directed solely to methods using microarray technology for ovarian cancer patients using normal ovarian epithelial cells and ovarian cancer cells as source for intracellular RNA, and detection of marker proteins (prostatin) from blood plasma or serum using antibody binding technology (see Abstract).

Applicant respectfully contends that the combination of the Kopreski reference, the Kang abstract and the Mok reference do not render obvious the instant claims due to multiple deficiencies, as follows:

1. None of the cited art teaches that extracellular RNA is present in pleural effusions.
2. None of the cited art teaches that apoptotic bodies are present in pleural effusions.
3. None of the cited art teaches methods for extracting, separating, isolating, or purifying apoptotic bodies from pleural effusion.
4. None of the cited art teaches that apoptotic bodies in pleural effusion contain RNA.

Applicant thus respectfully contends that the asserted rejection under 35 U.S.C. §103 has been overcome by amendment and traversed by argument, and requests that the Examiner withdraw this ground of rejection.

CONCLUSIONS

Applicant believes that all pending claims are in condition for allowance, and respectfully request that the pending claims be passed to issue.

If Examiner Natarajan believes it to be helpful, she is invited to contact the undersigned representative by telephone at (312) 913-0001.

Respectfully submitted,
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Dated: December 14, 2009

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